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<b>13. SUPPLEMENTARY NOTES</b>						
<b>14. ABSTRACT</b> Traumatic brain injuries (TBI) are a common occurrence from roadside blasts of improvised explosive devices (IEDs). In the proposed cross-sectional study, we aim to apply neurobehavioral testing and advanced MRI techniques [task-activated functional MRI (fMRI) and diffusion tensor imaging (DTI)] to gain a comprehensive understanding of the neural changes underlying blast-related MTBI. We will accomplish this goal by conducting advanced neuroimaging (task-activated fMRI and DTI fiber tracking) and neurobehavioral testing (computerized assessment and standard neuropsychological testing) on 60 chronic trauma patients: 15 military MTBI patients who have experienced blast injuries, 15 civilian MTBI patients with mechanical closed head injuries, 15 military and 15 civilian patients with orthopedic injuries. Year one of the project has been devoted to the development of the necessary infrastructure for the execution of this complex multisite study. A number of development tasks have been undertaken, including hiring and training a new coordinator in Houston, developing uniform procedures for analysis of image data in Cleveland and Houston, and further developing the avenues for recruitment of subjects. Years two and three were devoted to the recruitment of subjects. We have recruited 63 subjects and acquired cognitive data from 62 and imaging data from 57 of these subjects. We completed recruitment of subjects in Houston are satisfied that the accrual of data is of high reliability and integrity. Over the next year, we will continue data analysis across the two study sites and Cleveland will continue to recruit subjects.						
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## **Table of Contents**

Introduction.....	3
Body.....	3
Key Research Accomplishments .....	4
Reportable Outcomes.....	5
Conclusion .....	5
References.....	5
Appendices.....	5
Supporting Data .....	5

## INTRODUCTION

Traumatic brain injuries (TBI) are a common occurrence from roadside blasts of improvised explosive devices (IEDs). Like civilian TBI, blast-related TBI can result from mechanical forces in which objects in motion strike the head or the head is forcefully put into motion and strikes an object. TBI from exposure to an explosive blast may also result from a third cause: barotrauma. Blasts produce wave-induced changes in atmospheric pressure, which in turn produce characteristic injuries to vulnerable bodily regions at air-fluid interfaces, such as the middle ear. It is unknown whether the neural and cognitive sequelae of blast-related TBI differ from those resulting from mechanically-induced TBI commonly observed in civilian accidents. Understanding the potentially unique sequelae of blast-related TBI is critical for accurate diagnosis and designing effective pharmacological and neurorehabilitation interventions.

In the proposed cross-sectional study, we aim to apply neurobehavioral testing and advanced MRI techniques [task-activated functional MRI (fMRI) and diffusion tensor imaging (DTI)] to gain a comprehensive understanding of the neural changes underlying blast-related MTBI. This will be accomplished by comparing neurobehavioral and neuroimaging findings obtained from military personnel who have experienced a blast injury with those obtained from civilians who have experienced TBI from motor vehicle accidents and from military and civilian control participants with orthopedic injuries. We will accomplish this goal by conducting advanced neuroimaging (task-activated fMRI and DTI fiber tracking) and neurobehavioral testing (computerized assessment and standard neuropsychological testing) on 60 chronic trauma patients: 15 military MTBI patients who have experienced blast injuries, 15 civilian MTBI patients with mechanical closed head injuries, 15 military and 15 civilian patients with orthopedic injuries.

## BODY

Year three of the project was devoted to the development of the data collection and establishing a new imaging data collection site at the MEDVAMC. A number of development tasks have been undertaken to develop cross-platform analyses to provide reliability in image analysis. The analysis of imaging data is underway. While there have been problems over the year, each of them has been successfully managed to the exacting standards of the Principal Investigators. This meticulous work has laid the groundwork for high integrity in data collection. Details regarding each of these tasks are provided below, broken down by category.

Staff Recruitment, Employment, Organization, Training. There were no changes in staff in Houston. All study team members have completed all necessary Baylor and VA annual training.

### Neuropsychological and Neurobehavioral Measures

All screening and outcome data have been collected; forms have been scored and entered into an Access database. All electronic files have been backed up on a local drive.

### MRI

- Brain Imaging Protocols: Combining brain imaging data across two research sites is a considerable technical challenge. Extensive work has been done to establish a good matching of the scan parameters and to confirm the acquisition of comparable, high quality images for the Cleveland Clinic, Houston HNL and MEDVAMC scanners (all are Siemens 3T Trio MRI scanners).
- The imaging contract with HNL expired in December 2010 and the Houston site's fMRI data acquisition was moved back to the MEDVAMC.
- fMRI, DTI, and MRI Volumetric Data Acquisition: On 4/26/2011 Dr. Erik Beall, a project physicist at the Cleveland Clinic, visited the Houston site and during that trip he met with the local examiners and reviewed data acquisition procedures, he examined the VAMC's scanner and other data acquisition hardware, he set

up and tuned pulse sequences, and he obtained MRI test data for quality assessment using a normal volunteer subject. Data obtained during the testing were generally of good quality and the VAMC scanner then went into use for data acquisition. Since that time scanning at the Houston site has been completed. As of 9/30/2011, the Houston center has imaged 14 military TBI subjects, 15 military orthopedic injury and uninjured control subjects, 14 civilian TBI subjects, and 14 civilian orthopedic injury control subjects. All image data are transferred and archived at the image analysis laboratories in both Houston and Cleveland.

- **fMRI Data Analysis:** Procedures for SPM image processing and data analysis are now in place for data acquired using the Sternberg and Stop Signal fMRI paradigms. The Houston site has fully processed and completed first level (i.e., single subject) analyses for 22 cases for the fMRI Sternberg task and 4 for the Stop Signal task. Seven cases had some type of problem with data quality, including image artifact (e.g., movement or weak signal), poor subject performance during the fMRI scan, or incomplete brain coverage. Cases with good quality performance and image data have been given higher priority for processing and the Houston site is currently focusing on processing and analysis of the Sternberg data, since this is paradigm where this site has special expertise. Quality of the processed data has been good and the results of the preliminary analyses are generally consistent with prior reports of brain activation during these tasks. **DTI, Volumetric MRI Data Analysis:** We are up to date in the analysis of MRI volumetric data of brain regions. In addition we are in the process of analyzing the DTI data.
- **Houston Recruitment:** We have recruited 17 military TBI subjects (all male), 15 military controls with the orthopedic injuries and uninjured (11 male/4 female), 16 civilian TBI (9 male/7 female), and 15 civilian OI (9 male/6 female) subjects.

## KEY RESEARCH ACCOMPLISHMENTS

At this point in the project, the key accomplishments have been the completion of recruitment of the subjects in Houston (63 subjects were recruited with a goal of 60); 57 of those 63 were scanned. To summarize, key accomplishments have been:

- Finishing recruiting in Houston with a total of 63 subjects.
- Neuropsychological and Neurobehavioral outcome data collected for 62 subjects.
- fMRI, volumetric MRI, and DTI scanning completed for 57 subjects.
- Relocating imaging data collection back to the MEDVAMC.
- Development of complementary procedures for analysis of the fMRI data.
- Completing first level analyses for 22 cases for the fMRI Sternberg task and 4 cases for the Stop Signal task

## **REPORTABLE OUTCOMES**

Initial analyses indicate that the image data that have been acquired are of generally good quality and that the obtained activation patterns are meaningful. Houston data collection has been completed, analysis procedures are in place, and our efforts will now be directed towards completing group (i.e., second level) analyses to address the objectives of this study and generate reportable outcomes.

## **CONCLUSION**

The first year of the project was devoted to creating a viable infrastructure to support the collection of data across multiple sites. The second and third years of the project were devoted to the recruitment of subjects. Houston has completed recruitment of all subjects and is continuing with the data analysis. Our efforts will now be directed towards completing group (i.e., second level) analyses to address the objectives of this study and for dissemination of those findings.

## **REFERENCES**

There are currently no references to report, but publication of the study findings will now be a major focus.

## **APPENDICES**

None at this time

## **SUPPORTING DATA**

None at this time